TITLE: Synthesis of lunularic acid derivatives as chemopreventive agents

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10015525	A1	20011011	DE 2000-10015525	20000330 <--

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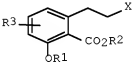
OTHER SOURCE(S): MARPAT 135:303727

GI



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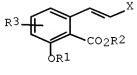

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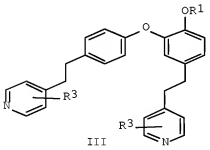

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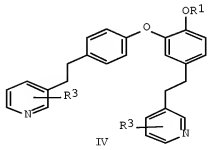


IV

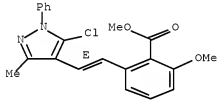
AB Lunularic acid derivs. [I-IV; X = (un)substituted mono or polycyclic (hetero)aryl; R1, R2 = alkyl, alkenyl, mono or polycyclic aryl; R3 = F, Cl, Br, I, amino. alkylamino, aminoalkyl, OH, carboxyl, alkoxycarbonyl, carbamoyl, aryl, acyloxy, etc.] are prepared which are suitable as chemopreventive agents. Thus, lunularic acid derivative II [R1 = R3 = H, R2 = Me, X = Ph (V)]

was prepared via Wittig reaction between (3-acetoxy-2-methoxycarbonyl)benzyl-triphenyl-phosphonium bromide and benzaldehyde. V was tested for chemopreventive properties (IC50 = 0.087 μM vs. Cyp1A1 in Hepa1c1c7 mouse hepatoma cells; 40% inhibition of DMBA-induced preneoplastic lesions in mice thymus gland culture; IC50 = 7.2 μM for inhibition of quinone oxidoreductase induction).

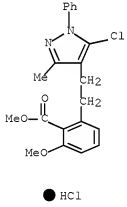
IT *365542-56-9P 365542-57-0P 365542-58-1P*
365542-59-2P 365542-60-5P 365542-61-6P
365542-74-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthetic derivs. of lunularic acid and their therapeutic use)

RN 365542-56-9 ZCAPLUS
CN Benzoic acid, 2-[(1E)-2-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethenyl]-6-methoxy-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

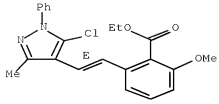


RN 365542-57-0 ZCAPLUS
CN Benzoic acid, 2-[2-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl]-6-methoxy-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

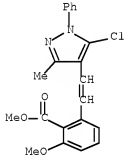


RN 365542-58-1 ZCAPLUS
CN Benzoic acid, 2-[(1E)-2-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethenyl]-6-methoxy-, ethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

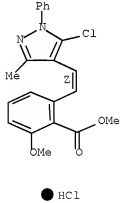


RN 365542-59-2 ZCAPLUS
CN Benzoic acid, 2-[2-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethenyl]-6-methoxy-, methyl ester (9CI) (CA INDEX NAME)

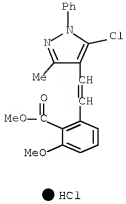


RN 365542-60-5 ZCAPLUS
CN Benzoic acid, 2-[(1Z)-2-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethenyl]-6-methoxy-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 365542-61-6 ZCAPLUS
CN Benzoic acid, 2-[2-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethenyl]-6-methoxy-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



RN 365542-74-1 ZCAPLUS
CN Benzoic acid, 2-[2-(5-chloro-3-phenyl-4-isoxazolyl)ethenyl]-6-methoxy-, methyl ester (9CI) (CA INDEX NAME)